REMARKS

Claims 79-83, 85-117, 122-131 are pending in this application. Claims 1-78, 84, and 118-121 have been canceled without prejudice. Applicants reserve the right to file one or more divisional, continuation, or continuation-in-part applications directed to any withdrawn or canceled subject matter. Claim 98 was amended to correct a typographical error. Claim 110 was amended to correct the claim identifier. Claims 130-131 have been added. Support for the new claims may be found throughout the application, for example, at page 11, first full paragraph.

No new matter has been added by the amendments.

I. The Objection of Claim 110 Is Rendered Moot

Claim 110 was objected to because an incorrect claim identifier was used. Applicants have amended claim 110 herein reciting the correct claim identifier, "currently amended," as recommended by the Examiner. Accordingly, this objection is rendered moot and withdrawal thereof is respectfully requested.

II. The Rejection Under 35 U.S.C. § 112, First Paragraph Should be Withdrawn

Claims 88 and 96 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Action states that the claims allegedly contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claim 88 encompasses, *inter alia*, a recombinant recognition molecule comprising the amino acid sequences set forth in (a)-(f), wherein (a) comprises SEQ ID NO. 1 or an equivalent canonical structural variant thereof; (b) comprises SEQ ID NO. 3 or an equivalent canonical structural variant thereof; (c) comprises SEQ ID NO. 5; (d) comprises SEQ ID NO. 7 or an equivalent canonical structural variant thereof; (e) comprises SEQ ID NO. 9; and (f) comprises SEQ ID NO. 11 or an equivalent canonical structural variant thereof; wherein the recognition molecule specifically binds to a glycosylated MUC1 tumor epitope. Claim 96 encompasses, *inter alia*, a recombinant recognition molecule comprising the amino acid sequences set forth in

(a)-(f), wherein (a) comprises SEQ ID NO. 2 or an equivalent canonical structural variant thereof; (b) comprises SEQ ID NO. 4 or an equivalent canonical structural variant thereof; (c) comprises SEQ ID NO. 6; (d) comprises SEQ ID NO. 8 or an equivalent canonical structural variant thereof; (e) comprises SEQ ID NO. 10; and (f) comprises SEQ ID NO. 11 or an equivalent canonical structural variant thereof; wherein the recognition molecule specifically binds to a glycosylated MUC1 tumor epitope.

According to the Office Action, the specification discloses specific variants of SEQ ID Nos. 13-31, but "does not provide sufficient written description as to the structural features of the claimed genus of antibodies and the correlation between the chemical structure and function of the genus of antibodies." (Office Action at p. 3). The rejection presents arguments asserting that "minor structural differences even among structurally related compounds can result in substantially different biology, expression and activities" and that "[e]ven minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function." (*see* Office Action at pages 4-6). The rejection argues that "applicant has not even disclosed a single species encompassed by the highly variant genus nor is there disclosure of the common attributes or features (i.e., residues) that are essential for activity or those which are non-essential." (Office Action at p. 8). The rejection concludes that "only antibodies comprising the specific sequences in claims 122-129, but not the full breadth of the claim meets the written description provision of 35 U.S.C.§ 112, first paragraph."

Applicants respectfully disagree and traverse the rejection for at least the following reasons. Applicants submit that the specification provides those with skill in the art at the time the invention was made with the information needed to determine whether a recombinant recognition molecule comprising an equivalent canonical structure variant of the claim-designated sequences would be encompassed by the present claims. Indeed, each of claims 88 and 96 provide both structural and functional elements, which are adequately claimed and described in the specification, to show possession of the invention.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116. The written description requirement for a claimed genus

may be satisfied through sufficient description of a representative number of species. *Regents of the University of California v. Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 (Fed. Cir. 1997). A "representative number of species" means that the species which are adequately described are representative of the entire genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]." See *Enzo Biochem, Inc. v. Gen-Probe, Inc., 323 F.3d 956, 969-70, 63 USPQ2d 1609, 1617 (Fed. Cir. 2002)*, 323 F.3d at 966, 63 USPQ2d at 1615.

However, description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. See, e.g., *Vas-Cath*, 935 F.2d at 1563, 19 USPQ2d at 1116; *Martin v. Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972) (stating "the description need not be in *ipsis verbis* [i.e., "in the same words"] to be sufficient").

First, the structural components are set forth in the recitation of the actual SEQ ID NOs of each of the components. For example, claim 88 is directed to a recombinant recognition molecule comprising the amino acid sequences set forth in (a)-(f), wherein (a), (b), (d), or (f) comprise SEQ ID NO: 1, 3, 7, 11, respectively, or an equivalent canonical structure variant thereof, and (c) and (e) comprise SEQ ID NOs: 5 and 9, respectively. Similarly, claim 96 is directed to a recombinant recognition molecule comprising the amino acid sequences set forth in (a)-(f), wherein (a), (b), (d) and (f) comprise SEQ ID NO: 2, 4, 8, or 11, respectively or an equivalent canonical structure variant thereof, and (c) and (e) comprise SEQ ID NO. 6 and SEQ ID NO. 10, respectively. Therefore, claims 88 and 96 are structurally defined by their sequence identification numbers.

In addition, the specification provides guidance to one skilled in the art at the time the invention was made to make and identify equivalent canonical structural variants according to invention. For example, the specification defines "equivalent canonical structural variants":

> According to the invention, equivalent canonical structure variants are understood to be amino acid sequences differing from the initial sequences to such an extent that at least one amino acid is replaced in well-defined positions without changing the canonical class." (Specification at p. 13, first full paragraph.)

In this respect, the specification provides (1) appropriate amino acid substitutions for the sequences and (2) methods of determining how canonical classes are defined. For example, at page 11, the specification provides that in a preferred embodiement, "single amino acids are replaced by amino acids having analogous physicochemical properties which, advantageously, do not fundamentally change the three-dimensional structure of the binding domain in the recognition molecules, so that the MUC1 specificity of the recognition molecules is retained." (Specification at p. 11) The application goes on to describe "[a]mino acids having analogous physicochemical properties in the meaning of the invention" in the six separate groups illustrated in Table 1. (Specification at 11-12.)

In addition, the specification describes canonical classes:

> By analyzing the loop conformations of the hypervariable regions (complementarity determining regions, CDRs) in the light and heavy chains of antibody molecules, so-called canonical classes have been defined [Chothia, Lesk, 1987; Chothia et al., 1986, 1989, 1992; Wu, Cygler, 1993]. (Specification at 13, first full paragraph.)

Antibody modelling described in the above-cited references allowed one skilled in the art at the time the invention was made to determine whether or not a particular sequence would be an "equivalent canonical structural variant" within the scope of the invention. For example, Applicants note that antibody modelling requires only that the Fv be modelled and that the constant region be conserved. Moreover, for the majority of the Fv itself, the framework is highly conserved in structure between different antibodies, and can be modelled using the most sequence-homologous framework. For CDR modelling, 5 of the 6 CDRs (all except H3) frequently fall into one of between 2 and 6 structure classes ("canonical classes"), a set for each CDR. (*See* Chothia and Lesk, *J. Mol. Biol.*, 1987, 196, p. 901 "Canonical structures for the hypervariable loops of immunoglobulins"; Chothia *et al.*, *Nature* 1989, 342, p. 877 "Conformations of immunoglobulin hypervariable regions," provided as references C6 and C4, respectively in the Information Disclosure Statement filed September 20, 2006.) These references support the notion that members of a canonical class all have approximately the same backbone conformation. This is particularly determined by the loop length and the presence of a number of key residues, both in the CDR and the framework, which hold the CDR in a given conformation by hydrogen bonding, electrostatic and hydrophobic interactions. Moreover, in order to model an unknown CDR, the sequence is examined, the appropriate canonical class is

assigned, and the most sequence-homologous known CDR is used. Accordingly, based on information known at the time the present application was filed, the skilled artisan knew how to determine variants that would constitute an "equivalent canonical structural variant" based on known antibody modelling methods.

Finally, the claims further provide that the claim-designated recognition molecule binds to a glycosylated MUC1 tumor epitope. The specification provides an adequate description to allow a skilled artisan to test whether a recognition molecule having an equivalent canonical structural variant would be encompassed by the present claims. For example, the specification describes that "specific binding of glycosylated MUC1 tumor epitope is understood to be binding of the recognition molecules of the invention comprising a combination of the following binding properties" set forth as (a)-(h) on pages 4-6. These attributes provide the skilled artisan with the information needed to determine if a molecule "binds to a glycosylated MUC1 tumor epitope" within the scope of the present invention.

In conclusion, Applicants respectfully submit that the specification provides an adequate description of the claimed invention, including the structural elements of sequences, a description of appropriate amino acid substitutions, known methods of determining canonical classes and "equivalent canonical structural variants," and assays to assess if a recognition molecule binds to a glycosylated MUC1 tumor epitope. The totality of this information requires a conclusion that the full scope of the present claims was in the possession of the inventors at the time the claimed invention was made. Based on at least the arguments set forth above, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 112, first paragaph be reconsidered and withdrawn.

Nevertheless, solely in an effort to expedite the prosecution of this aplications, Applicants have added new claims 130 and 131. Claim 130 provides, *inter alia*, a recombinant recognition molecule comprising the amino acid sequences set forth in (a)-(f), wherein (a) comprises SEQ ID NO. 1 or a variant thereof having a single amino acid substitution; (b) comprises SEQ ID NO. 3 or a variant thereof having a single amino acid substitution; (c) comprises SEQ ID NO. 5; (d) comprises SEQ ID NO. 7 or a variant thereof having a single amino acid substitution; (e) comprises SEQ ID NO. 9; and (f) comprises SEQ ID NO. 11 or a variant thereof having a single amino acid substitution; wherein the recognition molecule specifically binds to a glycosylated MUC1 tumor epitope. Claim 131 encompasses, *inter alia*, a recombinant recognition molecule comprising the amino acid sequences set forth in (a)-(f),

wherein (a) comprises SEQ ID NO. 2 or a variant thereof having a single amino acid substitution; (b) comprises SEQ ID NO. 4 or a variant thereof having a single amino acid substitution; (c) comprises SEQ ID NO. 6; (d) comprises SEQ ID NO. 8 or a variant thereof having a single amino acid substitution; (e) comprises SEQ ID NO. 10; and (f) comprises SEQ ID NO. 11 or a variant thereof having a single amino acid substitution; wherein the recognition molecule specifically binds to a glycosylated MUC1 tumor epitope. Support for the language "variant thereof having a single amino acid substitution" is provided throughout the specification including at page 11:

> In a preferred embodiment, modification of a recognition molecule is effected by one or more mutations in one or more amino acid sequences selected from SEQ ID Nos. 1 to 12, wherein single amino acid acids are replaced by amino acids having analogous physicochemical properties which, advantageously, do not fundamentally change the three-dimensional structure of the binding domain in the recognition molecules, so that the MUC1 specificity of the recognition molecules is retains. (Specification at p. 11)

As noted previously, Table 1 of the application describes "[a]mino acids having analogous physicochemical properties in the meaning of the invention" in the six separate groups. (Specification at pages 11-12). Therefore, the specification provides adequate guidance to the skilled artisan to identify the relevant structural information (sequence identification numbers) and suitable variations of such structures (*see* Table 1) to clearly show that Applicants were clearly in possession of the claimed invention. Applicants respectfully request examination of these new claims and an indication of allowability thereof.

III. Conclusion

Applicants believe that claims 79-83, 85-117, and 122-131 are allowable and respectfully request allowance thereof. The Examiner is invited to telephone the undersigned if that would be helpful to resolving any issues.

It is believed no fees are due; however, the commissioner is authorized to charge any fees and credit any overpayments to Deposit Account No. 50-5071 which may be due.

Respectfully submitted,

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